

# Exhibit 4



ANDA 091178

## REMS MODIFICATION NOTIFICATION

GenBioPro, Inc.

c/o

(b)(4)/TS-CI; (b)(6)/PPI

Attention:

(b)(4)/TS-CI; (b)(6)/PPI

Dear

(b)(4)/TS-CI; (b)(6)/PPI :

Please refer to your Abbreviated New Drug Application (ANDA) submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for mifepristone tablets.

### **RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS**

The Shared System (SS) REMS for mifepristone consists of elements to assure safe use, and an implementation system.

In accordance with section 505-1(g)(4)(B) of the FD&C Act, we have determined that your approved REMS for mifepristone must be modified to minimize the burden on the health care delivery system of complying with the REMS and to ensure that the benefits of the drug outweigh the risks.

This determination is based on a review of published literature, safety information collected during the COVID-19 PHE, FDA Adverse Event Reporting System (FAERS) reports, REMS assessment reports, and information provided by advocacy groups, individuals, the Applicants, and plaintiffs in ongoing litigation.

Your approved REMS must be modified as follows:

**Elements to Assure Safe Use:** We have determined that the requirement that mifepristone be dispensed only in certain healthcare settings, specifically clinics, medical offices, and hospitals (i.e., the “in-person dispensing requirement”) is no longer necessary to ensure the benefits of mifepristone outweigh the risks of serious complications associated with mifepristone that are listed in the labeling of the drug. Removal of the requirement for in-person dispensing will reduce the burden on the healthcare delivery system of complying with the REMS.

**Elements to Assure Safe Use:** Pursuant to 505-1(f)(1), we have also determined that an additional element to assure safe use is necessary to mitigate the risk of

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serious complications associated with mifepristone listed in the labeling of the drug. Modification of the Mifepristone REMS to allow dispensing of mifepristone by pharmacies requires the addition of certification of pharmacies that dispense the drug.

Your REMS must include elements to mitigate this risk, including at least the following:

- Healthcare providers who prescribe the drugs have particular experience or training, or are specially certified
- Pharmacies, practitioners, or health care settings that dispense the drug are specially certified
- The drug is dispensed to patients with evidence or other documentation of safe use conditions

The REMS must include an implementation system to monitor, evaluate, and work to improve the implementation of the ETASU (as outlined above). Include an intervention plan to address any findings of non-compliance with the ETASU.

The proposed REMS modification submission should include a new proposed REMS document and appended REMS materials, as appropriate, that show the complete previously approved REMS with all proposed modifications highlighted and revised REMS materials.

In addition, the submission should also include an update to the REMS supporting document that includes a description of all proposed modifications and their potential impact on other REMS elements. Revisions to the REMS supporting document should be submitted with all changes marked and highlighted.

Because we have determined that a REMS modification as described above is necessary to minimize the burden on the health care delivery system of complying with the REMS and to ensure that the benefits of the drug outweigh the risks, you must submit a proposed REMS modification within 120 days of the date of this letter.

Submit the proposed modified REMS as a Prior Approval supplement (PAS) to your ANDA.

Because FDA is requiring the REMS modifications in accordance with section 505-1(g)(4)(B) of the FD&C Act, you are not required to submit an adequate rationale to support the proposed modifications, as long as the proposals are consistent with the modifications described in this letter. If the proposed REMS modification supplement includes changes that differ from the modifications described in this letter, an adequate rationale is required for those additional proposed changes in accordance with section 505-1(g)(4)(A) of the FD&C Act.

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Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission:

**NEW SUPPLEMENT FOR ANDA 091178/S-000  
PRIOR APPROVAL SUPPLEMENT  
PROPOSED MAJOR REMS MODIFICATION**

Prominently identify subsequent submissions related to the proposed REMS modification with the following wording in bold capital letters at the top of the first page of the submission:

**ANDA 091178/S-000  
PROPOSED REMS MODIFICATION-AMENDMENT**

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format.

**SUBMISSION OF REMS DOCUMENT IN SPL FORMAT**

In addition to submitting the proposed modified REMS as described above, you can also submit the REMS document in Structured Product Labeling (SPL) format. If you intend to submit the REMS document in SPL format, include the SPL file with your proposed REMS modification submission.

For more information on submitting REMS in SPL format, please email [REMS\\_Website@fda.hhs.gov](mailto:REMS_Website@fda.hhs.gov).

If you have any questions, call

(b)(6)/PPI

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Sincerely,

*{See appended electronic signature page}*

(b)(6)/PPI

Center for Drug Evaluation and Research

U.S. Food & Drug Administration  
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Silver Spring, MD 20903  
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**This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.**  
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/s/  
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(b)(6)/PPI

12/16/2021 03:21:22 PM

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